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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

A positive family history, present in about 30% of breast cancer cases, has been shown to double a woman's risk of breast cancer. The genetic factors responsible are largely unknown, although the autosomal dominant, relatively high penetrant genes BRCA1/2 may account for 3%. It has been hypothesized that susceptibility genes of lower penetrance may also affect breast cancer risk, and a likely group of such genes are those that regulate the production, intracellular transport, and metabolism of estrogen. Previous studies of these susceptibility genes have not been conducted with women with high familial risk. This study is being conducted with identical twins with differing genetic risks (i.e. concordant for breast cancer pairs vs. discordant pairs) as well as unaffected controls. Initially we focused on genes related to estrogen metabolism (CYP17, CYP19, COMT, and HSD17B1) and carcinogen metabolism (GSTM1 and P1 and CYP1A1). In this no-cost extension we have expanded the number of genes to include AIB1 and p160, IGF-1, IGFBP-3, CYP3A4, GPR54, ER, PR, and COX-2.We will compare the frequency of haplotype SNPs and selected polymorphisms in these genes in 136 breast cancer concordant, 152 discordant, and 137 control women. We will use the high through-put Illumina system for these assays and will compare results from buccal smears and tissue samples for cases where we have both and results will be available within the next year. These results from the DNA from these twins will greatly add to knowledge about breast cancer susceptibility genes..

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4) INTRODUCTION

A positive family history, present in about 30% of breast cancer cases, has been shown to double a woman's risk of breast cancer(1), and this is true for postmenopausal as well as the premenopausal cases, among which the autosomal dominant, relatively high penetrant genes BRCA1 and BRCA2 are most prominent(2). It has been hypothesized that susceptibility genes of lower penetrance are more prevalent than among the latter, and a likely group of such genes are those that regulate the production, intracellular transport, and metabolism of estrogen (3), the common factor underlying most known predictors of breast cancer risk (4) (5) (6). Recent reviews have identified several candidate genes (7) (8) (9). We have chosen to focus on those genes related to estrogen metabolism and carcinogen metabolism.

In the estrogen metabolism pathway, four genetic polymorphisms have been described related to the CYP17 gene, the CYP19 gene, the COMT gene, and the HSD17B1 (or also called the EDH17B2) gene. For example, a polymorphism (called A2) on the CYP17 gene has recently been linked to higher endogenous estrogen levels and an earlier age at menarche (10). The same polymorphism was linked to increased risk of aggressive breast cancer, although one attempt to confirm this finding was unsuccessful(11). Genes related to carcinogen metabolism which have been linked to breast cancer risk include GSTM1 and P1 and CYP1A1. These studies, however, have not been conducted with women known to be at high familial risk, where the prevalence of the polymorphism may be expected to be higher, if it is associated with the development of breast cancer. This study proposes to take advantage of a unique subset of very high risk women in whom cumulative exposure to endogenous estrogen may play an especially important role in breast cancer etiology.

The identification of families to study these inherited genetic factors is more difficult because of the anticipated lower penetrance of the candidate genes and occurrence of more sporadic cases, especially among older women. The International Twin Study includes both breast cancer concordant and discordant identical twin pairs. The concordant MZ twin pairs represent families with a very high familial risk of breast cancer, while the MZ discordant twins are likely to represent non-heritable cancer. We plan to obtain DNA from subsets of these pairs as well as from control women without breast cancer (and without a family history of breast cancer) and to test for the genetic polymorphisms specified to determine if any are differentially associated with cases from twins with a high likelihood of heritable breast cancer (i.e. those from identical concordant pairs). This study should provide important clues regarding other genetic factors that may be associated with breast cancer etiology. Initial work on the project and the CYP17 laboratory work was funded under a grant from the California Breast Cancer Research Project (CA-BCRP).

A previous publication by the P.I. on epidemiological risk factors within the concordant for breast cancer identical twins, who are presumed to have a high genetic susceptibility, has indicated that factors associated with the onset of hormones at puberty may be especially critical (33) . The DNA from these twin pairs will be especially valuable in identifying additional genetic factors (and combinations of them) that may be related to breast cancer. Other studies

have relied on family history of breast cancer to identify women at high genetic risk, however this method may not be able to select for combinations of genetic factors in which two or more genes interact to increase risk. In these circumstances, the genes may be derived from both sides of the family, neither with a family history for breast cancer. Identical twins with both having breast cancer represent a group with high genetic susceptibility regardless of family history. Furthermore, since they are identical genetically, they also offer the opportunity to study gene x environment interaction. From the recently published study (33), it appeared that the earlier the puberty occurred the higher the risk of first breast cancer in the pair.

During the no-cost extension period we plan to increase the number of genetic factors studied using these twins with new high through-put technology that has recently become available at USC. Details are included in the section below under Task 4.

5) BODY

Technical Objectives and Work Accomplished in year 4:

Task 1: To complete follow-up of female identical twin pairs with breast cancer (Months 1-18)

1. *Continue follow-up begun under CA-BCRP grant*
2. *Hire Programmer, set up tracking database*
3. *Continue to mail follow-up forms with return envelope to last known address of twins. Enter data from responses.*
4. *Submit nonrespondent names to National Death Index.*
5. *Submit names of nonrespondent twins not known to be deceased to TRW/ Experian to obtain updated addresses. Resend follow-up forms.*
6. *Continue follow-up by phone calls, internet searches, and contact with relatives.*

It was previously reported that a data file was created from the International Twin Registry that selected all of the identical female twin pairs in which one or both members had been diagnosed with breast cancer. In total there are 1,491 identical pairs in this database and 1,199 of them were initially classified as discordant pairs, 263 as concordant, and 29 of uncertain concordance. A follow-up form was sent to all living members of all of the discordant pairs, and new breast cancers have been reported in the previously healthy twin of 62 of these pairs. Thus as a result of this information, there are now 338 concordant pairs and 1,153 discordant pairs. Follow-up efforts have consisted of mailing 1,883 follow-up forms to living twins in these pairs, and 1,029 have been returned completed. 260 were returned by the post office and 478 were not returned by either the twin or the post office. Tracing efforts were implemented to locate the nonrespondents. Follow-up of all nonrespondents will continue using the National Death Index. (This component was funded under the CA-BCRP grant).

Task 2: Identify new breast cancers and obtain medical record documentation and tissue blocks. (Months 6-20)

1. *When new breast cancer is identified, obtain medical consent form from twin or next of kin, and request records and tissue blocks from hospital*
2. *Follow-up requests with hospitals*

The goal of the study was to obtain genomic DNA from at least one member of 200 of the concordant pairs, from the case in 200 of the discordant pairs, and from 200 control women without a personal or family history of breast cancer. From a previous study, tissue blocks have been obtained from some of the breast cancer pairs (concordant and discordant). As a result of the follow-up effort, we have identified 62 previously discordant pairs in whom the unaffected member has developed breast cancer. Thus the number of concordant and discordant pairs has been adjusted to reflect the current status.

To participate in the study, the eligible participants are sent a letter describing the study along with the informed consent documents. Our study manager then calls the twin to go over the informed consent with her over the telephone. Then if she agrees to participate and donate the required tissue to the study, she then signs the informed consent form and mails it back to us. .

As of this time (8/2/04) the current numbers of MZ twins (and controls) in each subset with tissue and signed consent forms is the following:

	Concordant	Discordant	Controls
Number identified and either has agreed to participate or is still a potential participant*	169	892	137**
DOD consent signed and tissue/buccal smear available	**136**	**152**	**137**
(Number of above with buccal smear)	(42, with 13 having both buccal and tissue)	(20, with 8 having both buccal and tissue))	(137)
Tissue available from earlier study (and still attempting obtain signed informed consent)*	12	37	
Additional cases who could be sent buccal smear kit	21	786	

*after elimination of refusals, and deceased cases with no available tissue. Reasons for refusal included not interested, and too busy as well as the language that the DOD requires us to include in the informed consent regarding 'POTENTIAL FOR COMMERCIAL DEVELOPMENT RELATED TO RESEARCH'. The P.I. however is planning to recontact some of the 'soft' refusals, send them a copy of the recently published New England Journal article (33) and emphasize the importance of the study.

**this number increases with the addition of new cases

We currently have tissue or buccal smears and signed DOD informed consents for 136 concordant pairs, 152 discordant pairs and 137 controls. Due to difficulty in locating subjects it has taken more staff time than anticipated to obtain the current numbers and thus, we will complete the genetic analyses with these numbers of twins. We will still attempt to increase the number of concordant pairs in the study and convert some of the refusals.

Task 3: Obtain buccal smears from living member of case pairs when blocks not available (Months 1-20)

1. *If tissue blocks are no longer available from either member of the case pairs and there is a living twin, send letter to obtain buccal smear.*
2. *Send buccal smear kit and return mailing supplies and postage to these individuals.*

The procedures for obtaining buccal smears have been developed and kits have been assembled for this purpose. We are using Epicentre Technologies Master Amp Buccal Swab Brush. Two brushes are being sent to the selected cases (and controls) and they are asked to use one for each cheek. Once the swabs are returned to us they are being kept frozen until the laboratory analyses are done. To date we have collected buccal smears from 42 concordant pairs, 20 discordant pairs and 137 controls.

Task 3: Identify 200 control women and obtain buccal smear and risk factor questionnaire from each of them
(Months 1-20)

1. *Contact case pairs to obtain listing of unrelated breast cancer free potential control women selected from sisters-in-laws and friends.*
2. *Randomly select a women from this list and mail introductory letter.*
3. *Obtain buccal smear and risk factor questionnaire from each control woman through the mail.*

We have developed the protocol for selecting controls and this is working well. To date we have identified 137 controls and have obtained the buccal smear and short risk factor questionnaire from all of them.

Task 4: Laboratory analysis of DNA from tissue and buccal smears to identify polymorphisms in the specified breast susceptibility candidate genes
(Months 1-24)

1. *Finish CYP-17 analysis at Dr. Dubeau's Laboratory.*
2. *Extract additional DNA as necessary for the additional genetic tests.*
3. *Do additional tests for CYP19, COMT, HSD17B1, GSTM1, GSTP1, and CYP1A1.*
4. *Receive results and enter data into database.*
5. *Store tissue for future genetic studies.*

We had some difficulties in this area have worked to resolve the problems. This caused some delay in completing the genetic analyses. During this time period technological advances have been made in doing genetic assays, and costs per assay have been reduced. These developments have provided the opportunity to expand the scope of the genetic analyses that can be done with the available funding. We plan to do haplotype analyses of the genes (htSNPs) under study as well as continue to study the specific functional SNPs previously identified. In addition to the original genes we plan to other genes that have recently been identified has possibly being related to breast cancer susceptibility. These additional genes, listed in the table below include the co-activators AIB1 and p160, IGF related genes including IGF-1 and IGFBP-3 which regulates the amount of IGF-1, ER and PR genes, the COX2 gene related to inflammation, GPR54 which is related to the regulation of gonadotropins affecting onset of puberty[34], and CYP3A4*1B which plays a major role in testosterone metabolism and the high activity allele (i.e. CYP3A4*1B) may cause a larger drop in testosterone which may then increase the estradiol: testosterone ratio initiating the hormonal cascade that accompanies puberty[35].

Genes and number of SNPs to be assayed during no cost extension

Gene	Number htSNPs	Number other SNPs	Total SNPs
Original proposal:			
CYP1A1	9	1	10
CYP19	36	2	38
COMT	5	1	6
HSD17B1	10	2	12
CYP1A1	9	1	10
GSTP1	9	1	10
Additional genes:			
AIB1	40	1	41
P160	14		14
IGF-1	27		27
IGFBP-3	9		9
CYP3A4	14		14
GPR54	10		10
ESRalpha	58		58
ESRbeta	6		6
PR	20		20
COX-2	9		9
Total	285	9	294

The addition of the new genes plus the haplotype analyses will greatly expand the value of this study. We will include 10% duplicate samples in the assays to assess reliability of results.

These assays will be done using the Illumina System under the supervision of Dr. David Vandenberg (biosketch included) which is described below:

Illumina System Methodology

GoldenGate™ Assay and BeadArray™ Technology

Identification of multiple SNPs at the same time is performed using the GoldenGate™ Assay (Illumina, San Diego, CA). The assay utilizes a combination of the multiplexed oligonucleotide ligation assay (OLA) on genomic DNA (gDNA) and PCR amplification with universal primers. For each polymorphism, two allele specific oligonucleotides (ASO) are synthesized that contain 2 sequence motifs: common sequences at the 5' end for amplification of all targets (P1 and P2) and sequences at the 3' end that match the locus adjacent to the polymorphism with the final base of each oligonucleotide incorporating one of the 2 polymorphic bases. In addition to the 2 allele specific oligonucleotides a locus specific oligonucleotide (LSO) is synthesized that contains 3 sequence motifs: at the 5'end is sequence adjacent to the SNP being evaluated, a locus specific region in the middle of the oligonucleotide to identify the locus (Address), and sequences at the 3' end for amplification of all targets (P3). During the OLA each allele specific oligonucleotide will anneal to the region next to the corresponding polymorphism and each locus specific oligonucleotide will anneal to the adjacent region downstream of the polymorphism. When the last base of each ASO matches the polymorphic base DNA ligase will ligate the ASO and LSO oligonucleotides together. If a mismatch occurs the ligation step will not occur. Since each locus is independent, a large number of simultaneous annealings can occur provided there is no interaction between the combined oligonucleotides. At present combinations of up to 1536 loci can be performed at once. Next, the ligated oligonucleotides are amplified using generic primers that recognize the common domains within the ASO and LSO oligonucleotides. A total of 3 primers are used to amplify all of the loci at once: 2 primers that are labeled with distinct fluorochromes and are complementary to the P1 and P2 regions, respectively, for each ASO and 1 primer that is complementary to the P3 region of the LSO. Following PCR amplification of the ligation products, the products are denatured and hybridized to an array containing oligonucleotides with sequences complementary to the addresses used to mark each locus in the multiplexing reaction. The array contains approximately 50,000 independent sites with each of the addresses being represented at least 8 times. The array is then read to determine the fluorescent signal present at each address (BeadArray Reader, Illumina). The current system uses a 96-well plate format to detect the genotyping reactions for up to 1,536 assays at a time or 147,456 genotypes per plate. The robotics platform dedicated to the Illumina system is capable of processing at least 6 96-well plates per day for a throughput of over 800,000 genotypes per day. Data from the BeadArray Reader is downloaded to a Laboratory Information Management System (LIMS) and the genotypes are determined using Autogenopipe (Illumina). Genotyped data is retrieved from the LIMS database for analysis.

Assay Design

SNP design will be performed by Illumina from a list of SNPs provided to them for this project. The assay conversion rate for development of a successful assay from an identified SNP is approximately 97% when multiplexing 1,152 SNPs at a time and using "double-hit" SNPs

(Fan et al., 2003). Assuming a similar assay conversion rate for this study of known functional SNPs and HapMap identified SNPs we would expect 366 SNPs to work on the Illumina platform (97% of 378). Any SNPs that fail the Illumina design process will be analyzed using the TaqMan assay.

Quality Control

The Genomics Core Facility incorporates 2 levels of Quality control into all assays. Within the sample set a 5-10% blinded duplication of samples is created. Samples will be split and separate IDs generated prior to submitting the samples to the Genomics Core Facility. Results for an assay will not be analyzed if the duplicates do not have identical genotype and the cause for the discordancy (systematic or isolated) will be determined. A second level of QC is provided during sample setup. All DNA samples are diluted and stored in 96-well plates prior to aliquoting of DNA into assay plates. Only 93 samples are added to each 96-well plate with the remaining 3 empty wells serving as negative controls for the assay and as a unique fingerprint for each 96-well plate. These unique fingerprint wells allow the Genomics Core Facility to identify plate flips, or errors in the creation of assay plates.

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Task 4 Data analysis (Months 18-32)

1. *Link data on genetic factors to other information from twins and controls including risk factor information and other tumor related information when available (e.g. ER positivity)*
2. *Complete analyses of data to determine relationship of the specified polymorphisms to breast cancer susceptibility.*
3. *Submit papers and reports.*

The assays will be completed in the next year and the results analyzed and submitted for publication.

6) Key Research Accomplishments

a. We have obtained DNA and signed consent forms for 136 concordant pairs, 152 discordant pairs, and 137 controls.
b. DNA has been extracted from buccal smear samples.
c. We have developed plans for conducting the genetic assays using the Illumina System and have expanded the number of genes being studied.

7) Reportable Outcomes—none at this time.

8) Conclusions

We will have somewhat fewer cases and controls than originally planned, but we will expand the number of genetic studies that we will do on the cases and controls that we do have. Specifically, at minimum we will have DNA from 136 concordant pairs, 152 discordant pairs and 137 controls for a total of 425 samples. Nevertheless this should be sufficient to reach our research goals. We earlier had some unexpected problems with the PCR assays for CYP17, finding some inconsistencies in repeated samples. Thus we have spent additional time investigating the reasons for the discrepancies. Part of the problem may lie in the quality of the DNA that we have to work with for some of the samples. As a result, we will include duplicate samples for 10% of the samples done with the Illumina system to insure accuracy. In addition for some cases with tissue blocks we also have obtained buccal smears (13 concordant pairs and 8 discordant) and thus can compare the results of the two types of samples. Due to the clues from our recent publication regarding the importance of the puberty for the development of heritable breast cancer (33), we feel that this group of twins represents an extremely important and valuable group to study breast cancer susceptibility genes.

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10) APPENDICES

Current IRB approval

Copy of Dr. Vandenberg's biosketch.

Proposal **#001034**
Review Category: **C**

INSTITUTIONAL REVIEW BOARD
HEALTH RESEARCH ASSOCIATION
AND
INSTITUTIONAL REVIEW BOARD
UNIVERSITY OF SOUTHERN CALIFORNIA
SCHOOL OF MEDICINE

Date: 4/16/2004
To: **Ann S Hamilton, Ph.D.**
Assistant Professor
Preventive Medicine
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From: **Institutional Review Board No. 3**
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Los Angeles, CA 90033
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TITLE OF PROPOSAL:
BREAST CANCER SUSCEPTIBILITY GENES IN HIGH RISK WOMEN (DODBCRP)

Action Date: **4/6/2004** Action Taken: **Approved**
Committee: Institutional Review Board No. 3
Note:

The Continuing Review form and revised informed consent documents (dated 3/10/04) were reviewed and discussed by Institutional Review Board #3 (registration #00002881) at the convened meeting on April 6, 2004. This material was distributed to all members for their review prior to the meeting. The primary reviewer received a copy of the IRB file. The complete file was available for reference. Continuation of the study for 1 year was APPROVED by IRB #3 (7 votes for; 0 against; 0 abstentions). ***APPROVAL FOR THIS STUDY IS VALID APRIL 15, 2004 TO APRIL 14, 2005.***

The revised Version 1 informed consent document dated 3/10/04 was APPROVED.

The revised Version 1N informed consent document dated 3/10/04 was APPROVED.

The revised Version 2 informed consent document dated 3/10/04 was APPROVED.

The revised Version 3 informed consent document dated 3/10/04 was APPROVED.

The attached IRB approved informed consent documents dated 3/10/04, must be used for consenting study subjects. The informed consent forms have been stamped by the IRB office and will expire on April 14, 2005. You may not use the informed consent documents after the expiration date. You must submit a progress report (Continuing Review Form) sufficiently (one to two months) prior to the date of expiration of your study to permit review by the IRB. You will receive new informed consent documents to use for the following year if the Continuing Review of your project is approved.

The investigator is reminded of the requirement to submit any annual grant progress reports, non-competing continuations or competing renewals to the IRB review and approval.

HIPAA AUTHORIZATION APPLICABLE: Based on the documents submitted, the investigator is accessing, using or obtaining research subject/patient's identifiable health information (e.g., medical records, mental health information, lab reports, x-rays, tissue samples) from a) a health care provider (e.g., physician or other health care practitioner, hospital, clinic, nursing home); b) health plan (e.g., group health plan, insurance company, HMO); or c) health care clearinghouse (e.g., billing service) that is governed by the HIPAA privacy federal regulations and a waiver of authorization is not applicable.

An updated HIPAA-compliant authorization addendum is not attached to the informed consent. Please attach a HIPAA-compliant authorization addendum (dated 6/2003 or later) to your informed consent. The subject must sign and date both the authorization and the informed consent documents. A template addendum can be downloaded from any of the following web sites: at http://ccnt.hsc.usc.edu/irb/irb.html, the compliance website at www.usc.edu/compliance, and the USC policies web site at: http://policies.usc.edu. California Law requires that the HIPAA Authorization should remain a separate document from the Informed Consent. The Addendum must be edited specifically for this study only in the areas that allow such alteration. No other changes may be made.

Final approval to initiate this study has been given previously. You are authorized to conduct the research project as detailed in your protocol. Any proposed changes in the research study must be submitted, reviewed and approved by the IRB before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB should be promptly informed of the change following its implementation for IRB review.

You must conduct this research, and supervise the research staff involved in this research project in accordance with Federal, State, Local and Institutional policies concerning the use of human subjects in research. In conducting this research you must comply with IRB policies detailed in the most recent version of the IRB Policies and Procedures. If you do not have a copy of the IRB Policies and Procedures, do not continue this research, contact the IRB office immediately to receive it and review it carefully before you continue your research.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Photocopy this page or follow this format for each person.

NAME	POSITION TITLE
David J. Van Den Berg, Ph.D.	Research Assistant Professor of Urology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Marquette University, Milwaukee, WI	B.S.	1985	Biomedical Engineering
Stanford University, Stanford, CA	Ph.D.	1992	Genetics
Stanford University, Stanford, CA	Postdoctoral	1992-1993	Human Genetics

A. Positions and Honors

Positions and Employment

1998- Research Assistant Professor of Urology and Technical Director of Genomics Core Facility, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA
1996-1998 Research Assistant Professor of Medicine and Research Director of Medical Oncology Molecular Diagnostics Laboratory, College of Medicine, University of Illinois, Chicago, IL
1994-1995 Research Scientist I/II, Department of Molecular Biology, Systemix, Inc., Palo Alto, CA
1992-1993 Postdoctoral Research Fellowship in Human Molecular Genetics, Stanford University, Stanford, CA
1989-1990 National Eye Institute Pre-doctoral Training Fellowship, Stanford University, Stanford, CA
1985-1992 Graduate Research with Dr. Uta Francke, Stanford University, Stanford, CA
Thesis: Search for the Molecular Defect in Roberts Syndrome by Complementation
1985-1989 NIH Pre-doctoral Training Fellowship in Genetics, Stanford University, Stanford, CA

Honors and Awards

1985 B.S., Magna Cum Laude, Marquette University, Milwaukee, WI
1985 Top Scholastic Honors in Major Interest, Biomed. Eng., Marquette University, Milwaukee, WI
1985 Top Scholastic Honors, School of Engineering, Marquette University, Milwaukee, WI
1985 Sigma Xi, Science Honor Society
1982 Dean's Award, Outstanding Freshman, School of Engineering, Marquette University, Milwaukee, WI
1981-1985 Dean's Honor List, School of Engineering, Marquette University, Milwaukee, WI

B. SELECTED PEER-REVIEWED PUBLICALTIONS (in chronological order)

1. Le Marchand L, Haiman CA, van den Berg D, Wilkens LR, Kolonel LN, Henderson BE. (2004) T29C polymorphism in the transforming growth factor beta1 gene and postmenopausal breast cancer risk: the Multiethnic Cohort Study. Cancer Epidemiol Biomarkers Prev. 13, 412-5.
2. Wu AH, Tseng C-C, Van Den Berg D, Yu MC. (2003) Tea Intake, COMT Genotype, and Breast Cancer in Asian-American Women. Cancer Research 63, 7526-9.

3. Bretsky P, Haiman CA, Gilad S, Yahalom J, Grossman A, Paglin S, Van Den Berg D, Kolonel LN, Skaliter R, Henderson BE. (2003) The relationship between twenty missense ATM variants and breast cancer risk: the Multiethnic Cohort. Cancer Epidemiol Biomarkers Prev. 12, 733-8.
4. Wu AH, Seow A, Arakawa K, Van Den Berg D, Lee HP, Yu MC. (2003) HSD17B1 and CYP17 polymorphisms and breast cancer risk among Chinese women in Singapore. Int J Cancer 104, 450-7.
5. Koh WP, Yuan JM, Sun CL, Van Den Berg D, Seow A, Lee HP, Yu MC. (2003) Angiotensin I-converting enzyme (ACE) gene polymorphism and breast cancer risk among Chinese women in Singapore. Cancer Res 63, 573-8.
6. Ji Q, Chang L, Van Den Berg D, Stanczyk FZ and Stolz A. (2003) Expression Profile of Human AKR1C Family Members in the Prostate - Selective Reduction of AKR1C2 mRNA in Prostate Cancer. Prostate 54, 275-89.
7. Seow A, Yuan JM, Sun CL, Van Den Berg D, Lee HP and Yu MC. (2002) Dietary isothiocyanates, glutathione S-transferase polymorphisms and colorectal cancer risk in the Singapore Chinese Health Study. Carcinogenesis 23, 2055-2061.
8. Haiman CA, Bernstein L, Van Den Berg D, Ingles SA, Salane M and Ursin G. (2002) Genetic determinants of mammographic density. Breast Cancer Research 4, R5.
9. Hsieh CL, Oakley-Girvan I, Balise RR, Halpern J, Gallagher RP, Wu AH, Kolonel LN, O'Brien LE, Lin IG, Van Den Berg DJ, Teh CZ, West DW and Whittemore AS. (2001) A genome screen of families with multiple cases of prostate cancer: evidence of genetic heterogeneity. Am J Hum Genet 69, 148-58.
10. Platanias LC, Uddin S, Bruno E, Korkmaz M, Ahmad S, Alsayed Y, Van Den Berg D, Druker BJ, Wickrema A and Hoffman R. (1999) CrkL and CrkII participate in the generation of the growth inhibitory effects of interferons on primary hematopoietic progenitors. Exp. Hematology 27, 1315-1321.
11. Van Den Berg D, Sharma A, Bruno E and Hoffman R. (1998) Role of members of the Wnt gene family in human hematopoiesis. Blood 92, 3189-3202.
12. Bruno E, Horrigan S, Van Den Berg D, Fitting PR, Moss ST, Rozler E, Westbrook C and Hoffman R. (1998) The smad5 gene is involved in the intracellular signalling pathways which mediate the inhibitory effects of transforming growth factor-□ on human hematopoiesis. Blood 91, 1917-23.
13. Carella AM, Cunningham I, Lerma E, Dejana A, Benvenuto F, Podesta M, Celesti L, Chimirri F, Abate M, Vassallo F, Figari O, Parodi C, Sessarego M, Valbonesi M, Carlier P, Prencipe E, Gatti AM, Van Den Berg D, Hoffman R and Frassoni F. (1997) Mobilization and transplantation of Philadelphia-negative peripheral-blood progenitor cells early in chronic myelogenous leukemia. Journal of Clinical Oncology 15, 1575-82.
14. Van Den Berg D, Wessman M, Murray L, Tong J, Chen B, Chan S, Simonetti D,King J, Yamasaki G, DiGiusto R, Carella A, Frassoni F, Godin NC, Snyder D, Sciecinski I, Negrin R, Diesseroth A, Tsukamoto A, Gearing D, Reading C and Hoffman R. (1996). Leukemic burden in subpopulations of CD34+ cells isolated from the mobilized peripheral blood of γ-interferon resistant or intolerant patients with chronic myeloid leukemia. Blood 87,4348-57.
15. Tsukamoto AS, Van Den Berg D, Reading C, Tong J, Murray L, Carella A, Frassoni F, Snyder D, Herzig G, Gorin C, LaPorte J, Negrin R, Blume H, Cunningham I, Claxton D, Deisseroth A and Hoffman R. (1995). Isolation of both normal and leukemic cells within the hematopoietic stem cell compartment of CML mobilized peripheral blood. In: Autologous Stem Cell Transplant: Biological and Clinical Results in Malignancies, Harwood Academic Publishers, London.
16. Tsukamoto AS, Reading C, Carella A, Frassoni F, Gorin C, LaPorte J, Negrin R, Blume K, Cunningham I, Deisseroth A, Tricot G, Barlogie B, Tong J, Murray L, Van Den Berg D and Hoffman R. (1994). Biological characterization of stem cells present in mobilized peripheral blood of CML patients. Bone Marrow Transplantation 14, S3:S25-S32.

C. Other Support

ACTIVE

P30 CA 14089 — Peter A. Jones (PI) — 12/01/00-11/30/05 — 50%
NIH/NCI
Genomics Core Facility

The major goal of this facility is to assist Cancer Center members in genetic (polymorphism/mutation) and epigenetic (DNA methylation) analyses using high throughput technology to enable them to determine cancer predisposition and progression.
This project does not overlap with the proposed project.

R01 CA 43092 — Ross (PI) — 07/01/02-06/30/07 — 5%
NIH/NCI
Dietary Factors in the Etiology of Cancer in Shanghai

The major goal of this research project grant is to assess the roles of genetics and dietary factors in the cause of cancer in a cohort of 18,244 middle-aged men in Shanghai, China.
This project does not overlap with the proposed project.

R01 CA 74847 — Ursin (PI) — 01/01/99-12/31/04 — 10%
NIH/NCI
BRCA1, Oral Contraceptives and Hormonal Risk Factors

The major goal of this project is to evaluate the association between oral contraceptive use, hormonal factors and BRCA1 among breast cancer patients.
This project does not overlap with the proposed project.

PENDING

None

OVERLAP

None